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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
KAM, CHIH MIN

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/27/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/666,837	CORNELL-BELL ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the peptide PVIIA having an amino acid sequence set forth in SEQ ID NO:1, in which Xaa_1 is Arg, Xaa_2 is Hyp, Xaa_3 is Lys, Xaa_4 is Phe and Xaa_5 is His, in Paper No. 18 is acknowledged. The traversal is on the ground(s) that all the peptides claimed including the peptides set forth in SEQ ID NOs:2-25 which are analogs of PVIIA, all have activity against K channels; and there are limited numbers of peptides in the Markush group, thus, search and examination of the entire claim can be made without much burden. Applicants further assert that the use of BLAST (is the main method used at USPTO, but is incorrect, USPTO uses a Smith-Waterman algorithm for search) for searching generic SEQ ID NO: 1 and the native sequence would provide the homologous matches including the point mutant claimed in SEQ IDNOs: 2-25. This is not found persuasive because even the analogs of PVIIA have the activity against K channels, these peptides contain different amino acid sequences, thus, are patent ably distinct. Regarding the search of all peptides in the claim can be made without serious burden, a search for specific peptides must be made for all the sequences cited in the claim, and that a computer search for more than a single specific peptide constitutes a severe burden. The sequence databases are growing at an incredible rate, specific searches for each claimed sequence must be performed and search time and resources are not unlimited. At page 2 of the response (1st full paragraph) it is asserted that there are two criteria for restriction, it is noted and both criteria have been applied. Upon reconsideration, claims 1-19 along with SEQ ID NO: 1 will be examined, SEQ ID KNOWS: 2-25 are non-elected sequences, thus are

withdrawn from consideration. The requirement is still deemed proper and is therefore made FINAL.

Informalities

2. The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 5, line 30). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code from this page of the application and to review and appropriately amend by deletion any other instances of browser executable code. See MPEP § 608.01.

Claim Objections

3. Claims 1, 9, 10 and 18 are objected to because the claim contains recitation of non-elected sequences.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating hypoxia-induced depolarization or glutamate-induced excitotoxicity *in vitro* using kappa-conotoxin PVIIA (κ-PVIIA), does not reasonably provide enablement for a method for treating all disorders associated with radical depolarization of excitable membranes, cardiac ischemia, cerebral ischemia, asthma or ocular ischemia *in vivo* by administering a peptide of SEQ ID NO:1 or a derivative thereof. The specification does not

enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-19 encompass a method for treating disorders associated with radical depolarization of excitable membranes (Claims 1-4, 9), cardiac ischemia (claim 5, 10-19), cerebral ischemia (claim 6), asthma (claim 7) or ocular ischemia (claim 8) *in vivo* by administering a peptide of SEQ ID NO:1 or the derivative thereof. The specification, however, only discloses cursory conclusions (pages 3-4) without data supporting the findings, which state kappa-conotoxin PVIIA (κ-PVIIA), analogs and derivatives are used for activating ATP-sensitive K^+ channels and the opening of ATP-sensitive K^+ channels is useful for treating many disorders such as cardiac ischemia, cerebral ischemia, asthma and ocular ischemia. There are no indicia that the present application enables the full scope in view of treating a disorder associated with radical depolarization of excitable membranes by administering a peptide of SEQ ID NO:1 or a derivative thereof. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the derivatives of SEQ ID NO:1, the treating condition for a specific disorder such as cardiac

ischemia, cerebral ischemia, asthma and ocular ischemia, and the effects of the conotoxins in the treatment, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed methods in association with the variants except for the data that κ-PVIIA produces dose-dependent hyperpolarization, has protective effect against hypoxia induced depolarization *in vitro*, and is effective as a bronchodilator *in vitro* (Examples 4, 7, 8 10 and 11).

(3). The state of the prior art and relative skill of those in the art:

The prior art (references indicated at pages 13-14 of the specification) shows that K^+ channels openers are effective relaxants of airway smooth muscle reducing hyperactivity induced obstruction of intact airway, and they have beneficial vasodilatory effects in patients with angina pectoris and show great promise as cardioprotective agents (pages 13-14). However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the treating condition for a specific disorder associated with radical depolarization of excitable membranes and the effect of the peptide of SEQID NO:1 and the derivative thereof in the treatment for to be considered enabling for variants.

(4). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for treating disorders associated with radical depolarization of excitable membranes such as cardiac ischemia, cerebral ischemia, asthma or ocular ischemia in an individual by administering a peptide of SEQ ID NO:1 or the derivative

thereof. The specification indicates κ-PVIIA produces dose-dependent hyperpolarization, has protective effect against hypoxia induced depolarization *in vitro*, and is effective as a bronchodilator *in vitro* (Examples 4, 7, 8 10 and 11), however the specification does not demonstrate the use of κ-PVIIA or derivatives thereof in treating disorders associated with radical depolarization of excitable membranes in vivo, nor indicating the effect of the conotoxin peptide in the treatment. Moreover, there are no examples indicating the *in vivo* treatment. Furthermore, the specification has not shown how to extrapolate the in vitro data to in vivo effect. Although the general treating conditions such as the dosage of the conotoxin peptide has been cited in the specification (pages 11-12), the treating condition for a specific disorder such as cardiac ischemia, cerebral ischemia, asthma or ocular ischemia and the in vivo effect of the peptide on the disease is not shown. Since the specification fails to provide sufficient guidance on the treatment for a specific disorder associated with radical depolarization of excitable membranes using the conotoxin peptide, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of the conotoxin peptide.

(5). Predictability or unpredictability of the art:

The claims encompass treating disorder associated with radical depolarization of excitable membranes, however, the treating condition for a specific disorder and the effect of the peptide are not described in the specification, the invention is highly unpredictable regarding the outcome of the treatment.

(6). Nature of the Invention

Scope of the claims includes treating disorder associated with radical depolarization of excitable membranes, but the specification does not show how various disorders are treated using

the peptide of SEQ ID NO:1 and the derivative thereof. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed methods, and the guidance and the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the outcome of the treatment using the conotoxin peptide. Thus, practice of the full scope of the presently claimed invention based upon the current claims requires the practice of undue experimentation.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-10, 12, 14, 16 and 18 are indefinite because they lack essential steps as claimed in the process of treating disorders. The omitted step is the outcome of the treatment. Claims 2-9, 12, 14, 16 and 18 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

7. Claims 1-19 are indefinite because of the use of the term "a derivative of (a) or (b)". The term "a derivative of (a) or (b)" renders the claim indefinite, it is not clear what structure the derivative has, and how different the derivative is from the parent compound. Claims 2-9 and

11-19 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

8. Claims 9 and 18 are indefinite for because of the use of the term "may be substituted", "may be glycosylated", "may be". The term "may be substituted", "may be glycosylated", "may be" or "may be replaced" renders the claim indefinite, it is unclear whether the substitution, glycosylation or replacement occurs or not as to "may be". One interpretation of this type of language is that none of the modifications are present or some or all are present but is unclear because the above are representative of alternative interpretations of the claims. Claims 9 and 18 are also indefinite because of the use of the term "derivatives", it is not clear what structure the derivative has, and how different the derivative is from the parent compound. Regarding claims 9 and 18, the phrase "such as" or "e.g." renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

9. Claim 13 recites the limitation "the size of reperfusion infarct" in line 1. There is insufficient antecedent basis for this limitation in the claim. See also claims 15, 17 and 19.

Conclusion

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers

for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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January 24, 2003

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